

That which is claimed is:

1. A method for producing local analgesia in a subject having a site of local discomfort, said method comprising locally administering an effective amount of a tricyclic, second generation or third generation antidepressant to the site.

2. The method according to claim 1 wherein the antidepressant is a tricyclic antidepressant.

3. The method according to claim 1 wherein the tricyclic antidepressant has a structure:



wherein Z is a 7-membered ring, optionally containing 1 or 2 biocompatible
5 heteroatoms, or an 8-membered bicyclic ring,

Ar₁ and Ar₂ are optionally substituted aromatic rings fused to Z, and

R is an alkylamino or arylamino substituent, optionally an N-oxide derivative thereof.

4. The method according to claim 3 wherein the heteroatom is oxygen or nitrogen.

5. The method according to claim 3 wherein Ar₁ and Ar₂ are independently optionally substituted with a biocompatible halogen.

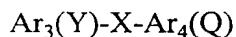
6. The method according to claim 3 wherein the alkylamino or arylamino substituent is an N-oxide derivative thereof.

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7. The method according to claim 3 wherein the alkylamino substituent comprises from 4 to 5 carbons atoms.
8. The method according to claim 7 wherein the alkylamino is a tertiary or secondary amino group.
9. The method according to claim 3 wherein R is selected from the group consisting of
- $(\text{CH}_2)_3\text{N}(\text{CH}_3)_2$,
 - $(\text{CH}_2)_3\text{NHCH}_3$,
 - $(\text{CH}_2)_3\text{N}(\text{CH}_3)_2$,
 - $\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2\text{N}(\text{CH}_3)_2$,
 - = $\text{CH}(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$,
 - $(\text{CH}_2)_3\text{NHCH}_3$, and
 - = $\text{CH}(\text{CH}_2)_2\text{NHCH}_3$.
10. The method according to claim 1 wherein the tricyclic antidepressant is selected from the group consisting of clomipramine, imipramine, amitriptyline, doxepin, desipramine, nortriptyline, amoxapine, maprotiline, trimipramine, and suitable combinations of any two or more thereof.
11. The method according to claim 1 wherein the tricyclic antidepressant is amitriptyline or desipramine.
12. The method according to claim 1 wherein the second generation or third generation antidepressant is selected from the group consisting of mirtazapine, venlafaxine, trazodone, bupropion, fefazodone, and suitable combinations of any two or more thereof.

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13. The method according to claim 12 wherein the second generation or third generation has the structure



wherein Ar_3 is an N-containing heterocyclic ring,

- 5 Y is either an aryl group fused to the heterocyclic ring or one or two substituents selected from alkyl, arylalkyl, arylalkyloxy, aryl and heteroaryl substituents comprising a total of about 4 to 8 carbons attached to Ar_3 , and attached to Q at a second nitrogen atom of Ar_4 .

14. The method according to claim 13 wherein the X is an alkyl group containing 3 carbons.

15. The method according to claim 13 wherein Ar_3 is a 1,2,4-triazole, Q is an heteroarylalkyl substituent containing 6 to 8 carbon atoms, and is substituted at the 4 position with Q.

16. The method according to claim 13 wherein the alkyl substituent contains 3 carbon atoms.

17. The method according to claim 13 wherein the benzene ring is substituted with a halogen selected from the group consisting of chlorine, bromine, and fluorine.

18. The method according to claim 1 wherein the tricyclic-antidepressant is desipramine.

19. The method according to claim 1 wherein the tricyclic-antidepressant is amitriptyline.

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20. The method according to claim 1 wherein the tricyclic-antidepressant is administered topically.
21. The method according to claim 1 wherein the antidepressant is administered as a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a polymer stabilized crystal, a powder, and an aerosol.
22. The method according to claim 17 wherein the antidepressant is administered by a method selected from injection, supersonic powder injection, and transdermal electroporation.
23. The method according to claim 1 wherein the antidepressant is administered encapsulated in a delivery system selected from the group consisting of a microsphere, a polymer stabilized crystal, and a liposome.
24. The method according to claim 1 wherein the analgesia suppresses pain caused by inflammation.
25. The method according to claim 1 wherein the analgesia suppresses neuropathic pain.
26. A composition for local administration comprising a tricyclic or heterocyclic antidepressant other than doxepine, and a vehicle suitable for topical administration.
27. The composition according to claim 26 wherein the antidepressant is a tricyclic antidepressant.

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28. The composition according to claim 26 wherein the tricyclic antidepressant has a structure:



wherein Z is a 7-membered ring, optionally containing 1 or 2 biocompatible
5 heteroatoms, or an 8-membered bicyclic ring,

Ar₁ and Ar₂ are optionally substituted aromatic rings fused to Z, and

R is an alkyl amino or aryl amino substituent, and optionally an N-oxide derivative thereof.

29. The composition according to claim 28 wherein the heteroatom is oxygen or nitrogen.

30. The composition according to claim 28 wherein Ar₁ and Ar₂ are independently optionally substituted with a biocompatible halogen.

31. The composition according to claim 28 wherein the alkylamino or arylamino substituent is an N-oxide derivative thereof.

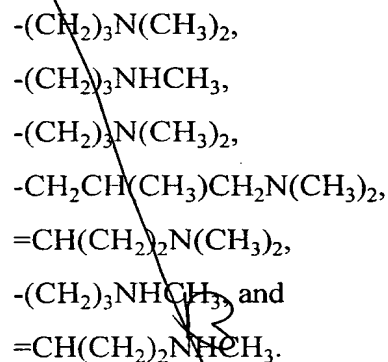
32. The composition according to claim 28 wherein the alkylamino substituent comprises from 4 to 5 carbons atoms.

33. The composition according to claim 32 wherein the alkylamino is a tertiary or secondary amino group.

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34. The composition according to claim 28 wherein R is selected from the group consisting of

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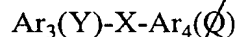


35. The composition according to claim 26 wherein the tricyclic antidepressant is selected from the group consisting of clomipramine, imipramine, amitriptyline, desipramine, nortriptyline, amoxapine, maprotiline, trimipramine, and suitable combinations of any two or more thereof.

36. The composition according to claim 26 wherein the tricyclic antidepressant is amitriptyline or desipramine.

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37. The composition according to claim 26 wherein the second or third generation antidepressant has a structure:



wherein Ar_3 is a substituted N-containing heterocyclic ring,

5 Y is either an aryl group fused to the heterocyclic ring, or one or two substituents selected from the group consisting of alkyl, alkyloxy, arylalkyl, arylalkyloxy, aryl, heteroaryl substituents, and combinations thereof comprising a total of about 4 to 8 carbons attached to Ar_3 ,

X is an alkyl group comprising 2 to 5 carbon atoms linking Ar_3 and Ar_4 ,

10 Ar_4 is a piperazine attached to X by a first nitrogen atom of Ar_4 , and

Q is a benzene ring optionally substituted with a biocompatible halogen and attached to Ar_4 at a second nitrogen atom of Ar_4 .

38. The composition according to claim 37 wherein the X is an alkyl group containing 3 carbons.

39. The composition according to claim 37 wherein Ar_3 is a 1,2,4-triazole substituted at the 4 position with the arylalkyloxy substituent containing 6 to 8 carbon atoms.

40. The composition according to claim 39 wherein the heteroarylalkyl substituent contains an oxygen atom.

41. The composition according to claim 37 wherein the benzene ring is substituted with a halogen selected from the group consisting of chlorine, bromine, and fluorine.

42. The composition of claim 23 further comprising an inert carrier.

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43. The composition of claim 42 wherein the inert carrier is selected from the group consisting of water, isopropyl alcohol, gaseous fluorocarbons, ethyl alcohol, polyvinyl pyrrolidone, propylene glycol, a fragrance, a gel-producing material, stearyl alcohol, stearic acid, spermaceti, sorbitan monooleate, methylcellulose, and suitable combinations thereof.
44. The composition according to claim 26 wherein the composition further comprises a penetration enhancing agent.
45. The composition according to claim 26 wherein the tricyclic-antidepressant is selected from the group consisting of desipramine, amitriptyline and a suitable combination thereof.
46. The composition according to claim 26 wherein the composition further comprises a penetration enhancing agent.
47. The composition according to claim 26 wherein the tricyclic-antidepressant is desipramine.
48. The composition according to claim 26 wherein the tricyclic-antidepressant is amitriptyline.
49. The composition according to claim 26 in a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a powder, a polymer stabilized crystal, and an aerosol.
50. The composition of claim 26 further comprising a neutralizing agent.

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51. The composition of claim 26 wherein the composition is formulated for local injection.

52. The composition according to claim 26 wherein the antidepressant is encapsulated in a slow release delivery vehicle.

53. The composition according to claim 52 wherein the delivery vehicle is selected from a liposome, a microcapsule, a polymer stabilized crystal.

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